

Remarks

Claims 1-13, 16, 18, 20 and 22-26 are pending in the instant application. Claims 13, 18 and 20 have been deemed withdrawn by the Examiner. Applicants have hereinabove cancelled claim 12 without disclaimer or prejudice to applicants' right to pursue the subject matter of this claim in a future application. In addition, applicants have hereinabove amended claims 1-4 and 11. Support for the amendments to claim 1 may be found, *inter alia*, in the subject specification on page 4, lines 27-30. The remaining amendments to the claims merely introduce minor grammatical and format changes. This Amendment does not involve any issue of new matter. Therefore, entry of this Amendment is respectfully requested such that claims 1-11, 16 and 22-26 will be pending and under examination.

Claim Objection

The Examiner objected to claim 11 because of the following informality: "post-menapausal" is misspelled. The Examiner required correction.

In response, applicants respectfully traverse. Nevertheless, without conceding the correctness of the Examiner's objection and in order to expedite prosecution of the subject application, applicants have hereinabove amended claim 11 such that it now recites the term "postmenopausal" instead of "post-menapausal." Applicants maintain that this amendment overcomes the Examiner's objection. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of objection.

Claim Rejection Under 35 U.S.C. §102(b)

The Examiner rejected claims 1-11 under 35 U.S.C. §102(b) as allegedly being anticipated by Masferrer et al. (WO98/22101) as evidenced by Bulun et al. (*J. Mol. Endocr.* 25: 35-42 (2000)).

In response, applicants respectfully traverse. Claim 1, as amended, provides a method for treating or preventing endometriosis in a patient in need of such treatment or prevention, comprising the administration of an effective amount of a cyclooxygenase-2 selective

inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381 (emphasis added).

Masferrer et al. does not teach the method of applicants' claimed invention. Specifically, Masferrer et al. does not teach use of the specific COX-2 inhibitors recited in claim 1, as amended. Therefore, Masferrer et al. fails to teach each and every element of claim 1.

In view of the above remarks, applicants maintain that claim 1, and claims 2-11 which depend therefrom, satisfy the requirements of 35 U.S.C. §102(b) and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claim Rejections Under 35 U.S.C. §103(a)

Claims 12 and 16

The Examiner rejected claims 12 and 16 under 35 U.S.C. §103(a) as allegedly unpatentable over Masferrer et al. (WO98/22101) in view of Riendeau et al. (*J. Pharm. Exp. Ther.* 296(2): 558-566 (2001)).

In response to the Examiner's rejection, but without conceding the correctness thereof, applicants point out that claim 12 has been cancelled. Thus, the rejection thereof is now moot. Applicants note that the elements of claim 12 have been incorporated into amended claim 1. Therefore, applicants will address the rejection of claim 12 as it now pertains to claim 1 below.

In response to the rejection of claim 16 and as it may apply to amended claim 1, applicants respectfully traverse and maintain that a *prima facie* case of obviousness does not exist with respect to any of the pending claims.

Claim 1 provides a method for treating or preventing endometriosis in a patient in need of such treatment or prevention, comprising the administration of an effective amount of a cyclooxygenase-2 selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib,

valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381. The COX-2 inhibitor under examination is etoricoxib as recited in claim 16, and the following remarks will be directed to this compound.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to the claim. First, the cited references, when combined, must teach or suggest every limitation of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Here, the cited references fail to support a *prima facie* case of obviousness. Specifically, Masferrer et al. when combined with Riendeau et al., fail to provide a motive to combine and a reasonable expectation of success.

Masferrer et al. does not teach or suggest the specific COX-2 inhibitor under examination, namely etoricoxib or any compound having a similar structure. Instead, Masferrer et al. suggest compounds having a particular structure as set forth in formulas I and II, recited on pages 6-26 therein, for use in treating endometriosis. As the Examiner conceded, the compounds encompassed by formulas I and II of Masferrer et al. do not include etoricoxib.

Riendeau et al. does not teach or suggest the use of etoricoxib to treat endometriosis. Riendeau et al. teach the use of etoricoxib to treat arthritis, hyperalgesia and pyresis. The use of etoricoxib to treat or prevent other diseases is unclear as evidenced on page 565, last paragraph of Riendeau et al., wherein the authors admit that further clinical studies with etoricoxib would be needed in order to explore the therapeutic potential of selective COX-2 inhibitors in inflammatory conditions, cancer and neurological disorders. Not only is the usefulness of selective COX-2 inhibitors to treat additional diseases/disorders unclear, nowhere do the authors mention the use of such inhibitors to treat endometriosis.

According to the MPEP §2143.01,

"[t]he mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007)."

As demonstrated above, there is simply no motivation or suggestion to combine the cited references to create applicants' claimed invention. The collection of cited references is the result of the Examiner's impermissible use of hindsight to combine these references based on knowledge of applicants' invention and underlying discovery. None of the references cited by the Examiner give any suggestion, motivation or "indication of which parameters [are] critical or [a] direction as to which of many possible choices is likely to be successful" to one skilled in the art with respect to the use of COX-2 inhibitors to treat endometriosis. (*In re O'Farrell*, 853 F.2d 894, 903 (Fed Cir. 1988)). Essentially, one skilled in the art would have had to conduct undue experimentation to achieve applicants' successful yet unexpected result. Devoid of any support to the contrary, an "invitation to try," which applicants do not concede exists, is considered inadequate support for an obviousness rejection. (*O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)).

In view of the above remarks, applicants maintain that claims 1 and 16 satisfy the requirements of 35 U.S.C. §103(a). Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims 22, 23, 25 and 26

The Examiner rejected claims 22, 23, 25 and 26 under 35 U.S.C. §103(a) as allegedly unpatentable over Masferrer et al. (WO98/22101) in view of Heinrichs (US 6,265,393, issued July 24, 2001).

In response to the rejection, applicants respectfully traverse and maintain that a *prima facie* case of obviousness does not exist with respect to any of the rejected claims.

Claim 22 provides a method for treating or preventing endometriosis in a patient in need of such treatment or prevention, comprising the administration of an effective amount of a

cyclooxygenase-2 selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381, and wherein the cyclooxygenase-2 selective inhibitor is concomitantly or sequentially co-administered with an oral contraceptive. The COX-2 inhibitor elected for examination is etoricoxib, and the oral contraceptive elected for examination is norethindrone as recited in claim 23.

Claim 25 provides a method for treating or preventing endometriosis in a patient in need of such treatment or prevention, comprising the administration of an effective amount of a cyclooxygenase-2 selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381, and wherein the cyclooxygenase-2 selective inhibitor is concomitantly or sequentially co-administered with a GnRH-agonist. The COX-2 inhibitor elected for examination is etoricoxib, and the GnRH-agonist elected for examination is leuprolide acetate as recited in claim 26.

The following remarks will be directed to these compounds.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to the claim. First, the cited references, when combined, must teach or suggest every limitation of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Here, the cited references fail to support a *prima facie* case of obviousness. Specifically, Masferrer et al. when combined with Heinrichs, fail to provide a motive to combine and a reasonable expectation of success.

As previously discussed *supra*, Masferrer et al. does not teach or suggest the specific COX-2 inhibitor under examination, namely etoricoxib or any compound having a similar structure. Instead, Masferrer et al. suggest compounds having a particular structure as set forth in

formulas I and II, recited on pages 6-26 therein, for use in treating endometriosis. As the Examiner conceded, the compounds encompassed by formulas I and II of MASFERRER et al. do not include etoricoxib.

Heinrichs does not teach or suggest the use of etoricoxib or any other COX-2 selective inhibitor to treat endometriosis. In fact, Heinrichs does not teach or suggest the use of any compound to treat endometriosis. Instead, Heinrichs describes coadministration of an estrogen agent and a progestin agent to prevent endometriosis *signs and symptoms* (emphasis added). Applicants are claiming the treatment and prevention of endometriosis itself, not the signs and symptoms of endometriosis. These are different diseases/disorders. Therefore, Heinrichs' disclosure is not relevant to the field to which applicants' invention as set forth in claims 22, 23, 25 and 26 is directed, and therefore, not prior art under 35 U.S.C. §103(a).

In addition, Heinrichs invention is directed to the coadministration of an estrogen agent and a progestin agent. Applicants' invention as set forth in claims 22, 23, 25 and 26 do not recite coadministration of both an estrogen agent and a progestin agent. Instead, applicants' invention as set forth in claims 22, 23, 25 and 26 recite the administration of either an oral contraceptive, such as a progestin agent, or a GnRH-agonist. Nowhere does Heinrichs teach or suggest the use of either a progestin agent alone or an estrogen agent alone, or either co-administered with a COX-2 selective inhibitor, to treat or prevent endometriosis.

According to the MPEP §2143.01,

"[t]he mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007)."

As demonstrated above, there is simply no motivation or suggestion to combine the cited references to create applicants' claimed invention. The collection of cited references is the result of the Examiner's impermissible use of hindsight to combine these references based on knowledge of applicants' invention and underlying discovery. None of the references cited by the Examiner give any suggestion, motivation or "indication of which parameters [are] critical or [a] direction as to which of many possible choices is likely to be successful" to one

skilled in the art with respect to the use of COX-2 inhibitors to treat endometriosis. (*In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). Essentially, one skilled in the art would have had to conduct undue experimentation to achieve applicants' successful yet unexpected result. Devoid of any support to the contrary, an "invitation to try," which applicants do not concede exists, is considered inadequate support for an obviousness rejection. (*O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)).

In view of the above remarks, applicants maintain that claims 22, 23, 25 and 26 satisfy the requirements of 35 U.S.C. §103(a). Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claim 24

The Examiner rejected claim 24 under 35 U.S.C. §103(a) as allegedly unpatentable over Masferrer et al. (WO98/22101). The Examiner conceded that Masferrer et al. does not teach the specific timing of the administration COX-2 selective inhibitors. However, the Examiner took notice that (a) all surgical procedures result in pain and inflammation, and (b) the administration of NSAIDs is effective in reducing pain and inflammation. The Examiner alleged that one of skill in the art would have been motivated to administer a COX-2 inhibitor in connection with an endometrial surgical procedure to treat pain because any type of surgery results in pain and inflammation, and COX-2 inhibitors are allegedly commonly known in the treatment of pain associated with surgery.

In response, applicants respectfully traverse and maintain that a *prima facie* case of obviousness does not exist with respect to any of the pending claims.

Claim 24 provides a method for treating or preventing endometriosis in a patient in need of such treatment or prevention, comprising the administration of an effective amount of a cyclooxygenase-2 selective inhibitor to said patient, wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of: rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502 and GW406381, and wherein the cyclooxygenase-2 selective inhibitor is administered perioperatively or as follow-up therapy to surgical removal of endometriotic implants. The COX-2 inhibitor under examination is etoricoxib, and the following remarks will be directed to this compound.

As previously discussed *supra*, MASFERRER et al. does not teach or suggest the specific COX-2 inhibitor under examination, namely etoricoxib or any compound having a similar structure. Instead, MASFERRER et al. suggest compounds having a particular structure as set forth in formulas I and II, recited on pages 6-26 therein, for use in treating endometriosis. As the Examiner conceded, the compounds encompassed by formulas I and II of MASFERRER et al. do not include etoricoxib.

With respect to what was known in the art, the Examiner alleged that one of skill in the art would have been motivated to administer a COX-2 inhibitor in connection with an endometrial surgical procedure in order to treat pain. Again, applicants note that claim 24 recites a method to treat and prevent endometriosis itself, not the symptoms of endometriosis, such as pain. These are different diseases/disorders that are governed by distinct physiological mechanisms, and are not interchangeable.

According to the MPEP §2143.01,

"[t]he mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007)."

As demonstrated above, there is simply no motivation or suggestion to combine the cited references to create applicants' claimed invention. The collection of cited references is the result of the Examiner's impermissible use of hindsight to combine these references based on knowledge of applicants' invention and underlying discovery. None of the references cited by the Examiner give any suggestion, motivation or "indication of which parameters [are] critical or [a] direction as to which of many possible choices is likely to be successful" to one skilled in the art with respect to the use of COX-2 inhibitors to treat endometriosis. (*In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)). Essentially, one skilled in the art would have had to conduct undue experimentation to achieve applicants' successful yet unexpected result. Devoid of any support to the contrary, an "invitation to try," which applicants do not concede exists, is considered inadequate support for an obviousness rejection. (*O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)).

In view of the above remarks, applicants maintain that claim 24 satisfies the requirements of 35 U.S.C. §103(a). Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection, and earnestly solicit allowance of the pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone her at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the large entity amount of such fee to Deposit Account No. 13-2755 referencing attorney docket number 21294P.

Respectfully submitted,

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